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Analysis of Humira, Electro-Acupuncture, and Pulsatile Dry Cupping on Reducing Joint Inflammation in Patients with Rheumatoid Arthritis

By Natalie Noll

Abstract

Humira, an anti-TNF drug aimed at decreasing inflammation in Rheumatoid Arthritis patients, can cause skin diseases from rashes to skin cancer. Humira works by blocking the chemical receptor RANKL which inhibits the production of osteoclasts. Osteoclasts are cells that attack and eat bone and cartilage therefore an inhibitory mechanism would cause inflammation.. By analyzing Humira's effect on the human body, Humira can be compared to other treatments such as electro-acupuncture and pulsatile dry cupping to determine the viability of these alternative treatment methods in regards to their abilities to decrease inflammation in Rheumatoid Arthritis patients through blocking RANKL. An analysis of these treatment methods can also be used to determine the safest treatment method.. Under close examination of scientific journals written on studies where patients and animals were treated with Humira, acupuncture, and cupping for inflammation due to arthritis, the data collected suggests that Humira, electro-acupuncture, and pulsatile dry cupping all decrease inflammation in the joints of Rheumatoid Arthritis patients. However, acupuncture causes the least harmful side-effects, with nausea and localized tingling being the most common complaints. On the other hand, localized bruising is caused by cupping and Humira is associated to an increased risk of cancer, heart failure and liver failure. Therefore, electro-acupuncture and pulsatile dry cupping are safer alternatives to Humira for the treatment of inflammation associated with Rheumatoid Arthritis. As a result, the data collected from this review supports that acupuncture has the same therapeutic effects as Humira, but is less deleterious and an overall better treatment method to Rheumatoid Arthritis compared to Humira.

Introduction

Rheumatoid Arthritis (RA) is a form of arthritis that leads to the inflammation of joints and is often associated with joint pain. RA specifically affects paired joints, joints found on both sides of the body such as the wrists, hips, and knees. Currently RA affects about 1% of the American population and is more prevalent in women than in men. Current research indicates that "pain is the second most common cause of loss of work in the United States" (Kim 135). Therefore, there has been incentive to develop new drugs that treat the joint inflammation and pain characteristic of RA. Drugs have been effective because

various drugs can be synthesized from a wide array of compounds to treat different types of 'pain' in specific areas of the human body. As a result, the medical field has turned to drugs to solve many issues related to the body, including RA. However, according to Kim (2004), "with all the advances of technology and treatments, it [pain] still remains a major problem in our society and continues to worsen" (135). Kim's statement suggests that drug treatments for pain may be minimally effective in terms of treating the 'pain' that Americans feel on a daily basis. Thus alternative treatment options, must also be considered when providing a treatment plan for a patient. Alternative treatments include utilizing alternative medicine, which is comprised of Traditional Chinese Medicine (TCM), a combination of "herbal remedies and acupuncture are the treatments most commonly used by TCM practitioners," (National Institute of Health 1) along with other forms of mind-body medicine that do not solely rely on drugs. Acupuncture, a form of TCM, has been practiced in China since before second century B.C., and has been used for centuries to cure pain. Today, "TCM is now practiced in one form or another by more than 300,000 practitioners in over 140 countries" (Scheid 10) and is taught in some European colleges, allowing TCM treatments to be available to many people throughout the United States, Europe, and Asia. Furthermore, new technology, in combination with these TCM treatments, has produced new forms of remedies such as electro-acupuncture, which provides an electric impulse to the needle while acupuncture is being performed, and pulsatile dry cupping, which "is a modernized technology using a mechanical device that generates a pulsatile vacuum with a pump," (Teut 2).

Treatments for the joint inflammation caused by RA requires TNF reduction. Humira is one of the most common drugs and it is used as a treatment for RA due to its ability to reduce TNF at high levels. While the prescription drug Humira has high levels of TNF reduction, the side effects, especially "increased risk for developing serious infections that may lead to hospitalization or death" (Physician's Desk Reference 1), can lead to infections such as Tuberculosis and an increased risk of cancer. These adverse reactions make Humira less desirable than the alternative therapies of electro-acupuncture and pulsatile dry cupping, whose side-effects include, "nausea or small tingling pain where the needle was injected" (Ouyang 508), and localized bruising. Furthermore, Humira is the most expensive treatment to have for one year, compared to acupuncture and pulsatile dry cupping (Food and Drug Administration 1). In addition,, even though Humira can be directly delivered to a patient through the mail and thus is easy to acquire, there is a growing number of facilities that offer acupuncture and cupping(Alderman B5). Also, of the three treatment methods, acupuncture is the most readily available treatment method because it is offered in every state, whereas the other two are not. Due to the less severe side effects associated with electro-acupuncture compared to Humira and the greater prevalence of

electro-acupuncture compared to pulsatile dry cupping, this review of research supports electro-acupuncture as the best choice for patients to reduce their inflammation and pain caused by Rheumatoid Arthritis.

Inflammation Due To Rheumatoid Arthritis

As stated above, RA currently affects about 1% of the American population, and is more prevalent in women than in men. One explanation is that women experience osteoporosis at a much high rate compared to men, resulting in greater bone damage. Inflammation in the joints is a symptom of RA, and is often treated with drugs, acupuncture, and/or cupping. In order to treat RA, the process that causes inflammation has to first be analyzed and studied.

According to G. Jie, a doctor at Suzhou Hospital of Traditional Medicine in China, et al. “TNF- α [a form of TNF] is an important physiological mediator of inflammation that mediates the host inflammatory response and leads to tissue damage, and is one of the most active inflammatory factors in RA” (207). This is further supported by Ouyang et al. in “Effect of Electro-acupuncture on Tumor Necrosis Factor- α and Vascular Endothelial Growth Factor in Peripheral Blood and Joint Synovia of Patients with Rheumatoid Arthritis.” (2011) The researchers stated that “it is well-known that high levels of tumor necrosis factor- α (TNF- α) and vascular endothelial growth factor (VEGF) could be detected in blood serum or joint synovia of patients with rheumatoid arthritis (RA)” (505). This supports the notion that higher TNF levels are always found when there is an increase in inflammation. These findings show that TNF and inflammation have a directly proportional relationship to each other and that any treatment that lowers inflammation should also lower the TNF levels in a patient’s body.

In a study on how TNF is related to osteoclast production, “Tumor Necrosis Factor Receptor-associated Factor 6 is an Intranuclear Transcriptional Co-activator in Osteoclasts,” by Bai et al. (2008), Bai et al. reported that “RANK is a member of the tumor necrosis factor (TNF) receptor superfamily, and as such, its cytoplasmic domain binds a number of TNF receptor-associated factors (TRAFs)” (30861). Since TNF and RANK have similar enough chemical structures they both activate RANKL, the cytoplasmic receptor of RANK. This is further supported in in, “Changes in Bone Mineral Density During Long-term Treatment with Adalimumab in Patients with Rheumatoid Arthritis: A Cohort Study,” by Kriekaert et al. (2012) when they state:

Generalized bone loss in osteoporosis goes beyond localized, periarticular bone loss in the affected joints. It is assumed that generalized and local bone loss share a common, inflammation-driven pathway, in which receptor activator of nuclear factor-B (RANKL) plays an important role (1).

Kriekaert et al. illustrate how TNF factors bind to RANKL to actively cause inflammation in the joints. This inflammation occurs when RANKL is

activated, and causes the production of osteoclasts. These osteoclasts then attack the bones and cartilage, breaking up the organic bone located there, causing inflammation as a result. In addition, Ouyang et al. stated that increasing TNF- α would “activate and damage the local vascular endothelial cells (VECs) to increase their permeability, and aggravate the local tissue inflammatory edema and infiltration” (505). The research presented by Bai et al., Krieckaert et al. and Ouyang et al. suggests that if TNF factors were decreased, there would be a decrease in osteoclast production since RANKL would be activated in smaller amounts.

The above research discussed TNF’s role as a ligand for RANKL; however, there is another chemical that acts as an antagonist to RANKL. Four and half LIM domain 2 (FHL2) also binds with RANKL, like TNF, except instead of activating RANKL, it inhibits it, thereby acting as a receptor antagonist. Bai et al. explain that:

Four and half LIM domain 2 (FHL2) is a LIM domain-only protein, not present in bone marrow macrophages (BMMs) but induced by RANKL, which binds TRAF6, thereby inhibiting its interaction with RANK (6).

The inhibition of RANKL therefore stops the body’s production of osteoclasts, which leads to the inhibition of osteoclast attack and destruction on the patient’s joints. Thus, the inhibition of RANKL may cause a reduction in inflammation. Consequently, FHL2 and RANKL have an indirect relationship. This means that in order to find a way to decrease inflammation through the RANKL pathway, either TNF factors must be reduced or FHL2 factors must be increased. Either mechanism will result in a decreased activation of RANKL, which will lead to a reduction in the number of osteoclasts that are produced by the body.

Prescription Drug Treatment of Rheumatoid Arthritis

When a patient is diagnosed with RA, the most common treatment method for the pain and inflammation is a prescription anti-TNF drug. One of the most common drugs on the market is Humira, in which its leading ingredient is the anti-TNF drug, adalimumab. However, Humira has many adverse effects. The side effects of this drug range from “headache, stuffy nose, sinus pain, [and] mild stomach pain” (Physicians’ Desk Reference 1), to a reduced immune system, which has caused some patients to develop skin lesions, lymphoma, allergic reactions, and the inability to form blood clots. The Food and Drug Administration (FDA) warns users on Humira’s prescription guidelines that “liver problems can happen in people who use TNF-blocker medicines. These problems can lead to liver failure and death” (3196923).

Currently, according to the Physician’s Desk Reference (PDR) (2012), “Humira is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving phys-

ical function in adult patients with moderately to severely active rheumatoid arthritis” because of its role of treating RA’s inflammation and joint pain (1). Binder et al. in, “TNF Inhibiting Therapy Preferentially Targets Bone Destruction but Not Synovial Inflammation in a TNF Driven Model of Rheumatoid Arthritis,” state that Humira works to lower the TNF that causes inflammation to occur because the inflammation is:

Retarded, by treatment with the anti-TNF antibody infliximab, even if clinical signs and symptoms of inflammation are not affected. Similar observations have been also made for two other TNF inhibitors, etanercept and adalimumab [Humira] (611).

The findings by Binder et al. are supported by their research that they conducted on the use of the anti-TNF drug Humira, and how it affected the osteoclast (OC) numbers that are found in the body. This is relevant because when TNF activates RANKL, osteoclasts are produced in the bone, therefore when OC numbers decrease, TNF levels are being lowered. The conclusion by Binder et al. was:

We found that TNF inhibition dramatically reduced pre-OC numbers in a dose depended manner [figure 1, B]. Moreover, TNF inhibition was effective in reducing pre-OC numbers not only in the absence, but even in the presence of RANKL [figure 2 D]. Taken together these data suggest that TNF inhibition mainly affects pre-OC differentiation rather than the development of mature OCs, at least under these conditions (611).

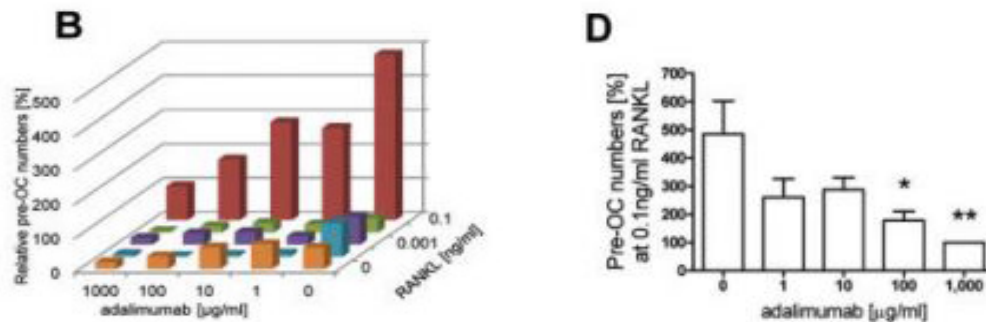


Figure 1 B: “Use of different concentrations of Humira on pre-OC numbers.
Figure 1 D: “Effect of TNF inhibition of pre-OC numbers” (Binder et al. 611).

Since TNF inhibitions only affect pre-OCs, this means that prior OC’s in the body will continue to be present and harm the joint. Humira, will stop any new OC’s from forming, decreasing inflammation over time. When OC’s are formed, they attack the bone and cartilage in the joints resulting in decreased bone mass density (BMD), as in Rheumatoid Arthritis patients. This was supported by Kriekaert’s et al. because they found that the “mean BMD change per year was 0.58% and 0.07% for the hip and lumbar spine, respectively, during a mean

follow-up period of 4 years” in experiments done with Humira (3). Therefore, the anti-TNF drug, Humira, helps decrease the OC production and retard the BMD loss in patients

Side-effects of Humira

Humira has many benefits, as well as many negative side effects such as a decrease in immune system functioning and an increased risk of cancer, liver disease, and heart failure. Although all of these side-effects are not experienced by over 50% of the patients that take Humira, common side-effects include “headache, stuffy nose, sinus pain, mild stomach pain; or pain, redness, itching, swelling, or bleeding where you injected the medication” (Physician’s Desk Reference 1). These common side effects, although less serious, can still be crippling to the daily activities of a patient. According to the National Institute of Health (NIH) “common adverse reactions (incidence >10%): infections (e.g. upper respiratory, sinusitis), injection site reactions, headache and rash” are prevalent in RA patients (1). Although these reactions are not life threatening, they do cause the patient discomfort, and should be taken into consideration when taking Humira. The side-effects that are life-threatening should not be taken lightly, since they are more likely to occur in patients that are older and already have a serious infection such as Crohn’s disease or heart disease.

The most problematic of these effects is the suppression of the patient’s immune system. According to the Physician’s Desk Reference (PDR), “patients treated with Humira are at increased risk for developing serious infections that may lead to hospitalization or death,” causing thousands of Humira patients to take other drugs to cure infections that they contract while on Humira (1). This risk of infection is supported by the Food and Drug Administration because “serious infection...even if your TB test is negative your doctor should carefully monitor you for TB infections while you are taking HUMIRA ” (Food and Drug Administration 3196923). This suggests that it is easier for a patient to contract tuberculosis while taking Humira. The risk of serious infection is important because many of the patients who are prescribed Humira are older, and already have a suppressed immune system. This means that for older adults, whom often are characterized by more compromised immune systems, may be at increased risk of contracting diseases such as “Tuberculosis (TB), invasive fungal, and other opportunistic infections, some fatal,” according to the National Institute of Health’s highlights of prescribing Humira information (2007 1). According to the PDR, “active tuberculosis (TB), including reactivation of latent TB...Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis... [and] bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria,” are repeatedly found in patients who are taking Humira, (1).

The diseases mentioned above, such as TB and fungal infections, may develop fairly quickly after taking Humira. In addition, Humira can cause cancer, which most likely will not develop in susceptible patients until after the patient has ceased taking Humira. This is supported in a study in “Lymphomatoid Papulosis in a Patient Treated with Adalimumab for Juvenile Rheumatoid Arthritis,” by Park in which the researchers stated that “TNF- blockers [including adalimumab/ Humira] used to treat inflammatory disorders are also believed to reduce host immune responses to malignancy, thereby indirectly increasing the risk of secondary cancers ” (261). In Park’s study, he also found that “to date, data from several studies and case reports have shown an increased incidence of lymphoma in patients treated with anti-TNF agents” (259). These cases of lymphoma are supported by the NIH (2007) in their prescription data when they state, “Malignancies are seen more often than in controls, and lymphoma is seen more often than in the general population” (1), and further supported by the FDA who found that besides lymphoma, other cancer such as “basal cell cancer and squamous cell cancer of the skin [occur in the patient]. These types of cancer are generally not life-threatening if treated but “people with RA, especially more serious RA, may have a higher chance for getting a kind of cancer called lymphoma” (3196923).



Figure 2: “Erythematous to brown nodules on the elbow and upper arm.” (Park 260)

This is important because according to the PDR (2012) “Humira is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis,” (1) and is therefore commonly prescribed to people with Rheumatoid Arthritis . However, Humira directly “increases your change of having a higher chance for getting a kind of

cancer called lymphoma” (Physician’s Desk Reference 3196923). Furthermore:

“Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including Humira. These cases have had a very aggressive disease course and have been fatal” (Physician’s Desk Reference 1).

This means that by taking Humira, it is possible to contract strains of rare forms of lymphoma which can cause death because little knowledge is known about the cancer’s treatment and its inability to cure it.

Besides cancer, there are other side-effects that are prevalent with the use of Humira. The liver is an important organ in the body because of its functions

of cleaning the blood, regulating blood clots, and producing bile. Humans are therefore unable to survive without a functioning liver. Thus, it is a problem that the FDA (2012) found that “liver problems can happen in people who use TNF-blocker medicines [Humira]. These problems can lead to liver failure and death” (3196923). By taking Humira, patients are at risk of liver damage, which is deleterious to normal liver functionality. In addition, another problem associated to Humira is “heart failure, worsening or new onset” (National Institute of Health 1). As a result, Humira should not be a choice drug for those people who already have heart disease or who are at risk of heart disease.

Furthermore, Humira is expensive, costing a patient without insurance coverage around \$4,507.36 a year because Humira is usually prescribed “usually every other week” (Food and Drug Administration 1). However, after receiving a prescription from your doctor, Humira can be mailed to your home, or picked up at any local pharmacy, making it easily accessible to almost any person in the United States as long as they can pay for the dosages . This suggests that Humira should be used as a first choice of treatment for patients who are home-bound or sedentary because they cannot receive treatments such as cupping or acupuncture, which require patients to go to outside-of-home facilities. However, for RA patients who are not restrained due to a sedentary lifestyle,, they should consider alternative treatment methods before resorting to Humira to prevent the potential onset of Humira induced disease.

How Electro-Acupuncture Works

Electro-acupuncture reduces inflammation caused by Rheumatoid Arthritis because it targets the TNF levels in the peripheral blood and the joint fluid,, thereby lowering TNF levels in the body and reducing joint inflammation.

Acupuncture has been used to treat pain and inflammation in people since the second century B.C.E. In the research paper, “Influence of Electroacupuncture on Tumor Necrosis Factor- α and Vascular Endothelial Growth Factor in Rats with Experimental Arthritis”, Jie et al. (2012) found that: Due to the universality and network profile of the cytokines in the pathological process of RA, the pathway for EA [electro-acupuncture] effect on TNF- α and VEGF reduction might be as the following four: the first is a direct inhibitory effect; the second is indirect inhibition, i.e., through the cytokines mutual coupling effect; the third is the role of chemokine generation; the last is the regulatory function of nerve-immune-endocrine system (208).

Jie et al. suggest that EA has a direct effect on the amount of TNF in the body. This claim is supported by his experiments, which showed that “synovial content were insignificantly different after treatment ($P>0.05$), suggesting the equivalent effects of EA and SN in lowering TNF- α contents” (3). Because TNF factors were lowered due to EA, this means that less RANKL was activated,

which resulted in a decrease in osteoclast production. This would lead to a decrease in inflammation, which was proven by a “reduction of stimulation caused by antigen in the whole body and local inflammation” (Jie et al. 2007).

Group	Case	Time	TNF- α	
			Blood	Synovia
EA	32	Pre-treatment	146.32 \pm 10.19	149.76 \pm 14.12
		Post-treatment	139.25 \pm 9.85*	142.75 \pm 13.67
		Lowering value	7.53 \pm 1.43 ^Δ	6.87 \pm 1.65
SN	31	Pre-treatment	147.02 \pm 10.33	148.81 \pm 14.06
		Post-treatment	141.26 \pm 10.46*	142.19 \pm 13.59*
		Lowering value	5.89 \pm 1.21	6.39 \pm 1.46

Table 1: “Comparison of TNF- α Contents in Blood and Synovia” (Ouyang 507).

Furthermore, in “Effect of Electro-acupuncture on Tumor Necrosis Factor- α and Vascular Endothelial Growth Factor in Peripheral Blood and Joint Synovia of Patients with Rheumatoid Arthritis,” Ouyang et al. (2011) described their patients as having “high acceptance,” referring to the fact that their patients had no or minimal discomfort with electro-acupuncture, and therefore did not stop treatment (508). “High acceptance” is important because, as a viable treatment for inflammation, EA must be used on as many different types of people with varying diseases and pain tolerance levels. The discomfort consisted of nausea or small tingling pain where the needle was injected. Ouyang et al. also observed that there was not any “adverse reaction related with the treatment [that] occurred during the observation period,” thus concluding that no allergic reactions or major health issues occurred (508). The one caveat to electro-acupuncture is that blood diseases could be passed between people who shared needles. Therefore, when receiving electro-acupuncture, it should be done in a medical facility that uses safe disposal and cleaning methods for objects that contact bodily fluids.

In terms of cost, the amount of money per week for acupuncture is drastically lower than paying for Humira, with “sessions with an acupuncturist running about \$65 to \$120, depending on where you live” (Alderman B5). With even the most expensive treatments costing \$300 a session, this corresponds to only \$3600 a year, an amount still about \$1,000 less than Humira treatment. However, many “acupuncture schools have clinics where you can be treated by supervised students at discounted rates of \$40 or so for one to two hours” (Alderman B5), which would decrease the costs of having acupuncture performed. These schools are located within every state of the United States, including some territories, and most offer reduced prices when students are performing the acu-

puncture. Therefore, if the patient has access to transportation, it is more likely that he or she can find a school that is sponsored by the American Association of Acupuncture and Oriental Medicine. There, the patient is able to receive cheaper acupuncture treatment, and therefore acupuncture should be considered as a treatment when compared to the prescription drug Humira.

How pulsatile dry cupping works

Pulsatile dry cupping is one way to treat Rheumatoid Arthritis patients because it can stimulate deep into the skin, affecting the acupuncture points, releasing chemicals in the body which will decrease the levels of TNF and inflammation

According to M. Teut et al. in “Pulsatile Dry Cupping in Patients with Osteoarthritis of the Knee – A Randomized Controlled Exploratory Trial,” cupping also comes in two different forms, dry and wet. Today, the most common form, and the one used in this study, is pulsatile dry cupping. Pulsatile dry cupping “is a modernized technology using a mechanical device that generates a pulsatile vacuum with a pump,” when the vacuum is applied to the area that has pain with a cup (2).



Figure 3: “Application of adaptable silicone cup at the knee” (Teut et al. 4).

By using modeling, Tham et al. in “Cupping: From a Biomechanical Perspective,” the researchers found that the stresses on the skin that are caused by the pulsatile dry cupping were found at:

The center of the cup ($r \frac{1}{4} 0 \text{ mm}$) and the compressive stresses just beyond the rim of the cup ($\delta r X25 \text{ mm}$) are increased for increasing vacuum pressure loads. For the vacuum pressures applied, the results also show that the effect of cupping does not extend beyond the area enclosed by the cup; at twice the cup diameter ($\delta r \frac{1}{4} 50 \text{ mm}$), the stresses at the fat-muscle interface are negligible (2188).

This pressure will ultimately cause the decrease in inflammation in the affected joints that the cupping is being applied to. Teut et al. postulated that “the level of the spinal cord may also be involved [in reduction of pain]: Manipulations may stimulate inhibitory receptive fields of the multi-receptive dorsal horn neurons” (8). Tham et al. further supported this theory because according to their theory:

AA (Acupuncture analgesia) is initiated by the stimulation of the small diameter nerves in muscles which then send impulses to the spinal cord. The

three neural centers, namely, the spinal cord, the mid-brain, and the pituitary are subsequently activated and release transmitter chemicals, such as endorphins and monoamines, which block the pain messages (2184).

This illustrated that the chemicals released by the Central Nervous System could act like FHL2, and act as antagonist to RANKL. This would inhibit the formation of osteocytes, which would then lead to the decrease of inflammation in a patient's body.

While cupping does decrease pain and inflammation overall in the area that the cup is being applied to, cupping of all types causes some damage to skin. According to Teut et al., cupping “may firstly influence chronic pain locally by deforming or even injuring the skin which stimulates A β fibers in painful but also distal skin regions” (8). This damage to the skin is primarily seen and characterized by Tham (2205) as:

Ecchymosis, a discolouration of the skin caused by the escape of blood into the tissue from ruptured blood vessels. This is a characteristic feature of the cupping treatment and takes the form of a circular lesion” (2192).



Figure 4: “Results of Cupping”
(Tham et al. 2191).

However, while pulsatile dry cupping can cause some skin discomfort through bruising, Tham et al. stated that cupping has one major advantage in that “transmission of blood-borne diseases can be avoided since skin is not penetrated” (2191). This makes cupping superior to acupuncture and Humira, because in both acupuncture and Humira, a needle must puncture the skin in order to stimulate perform the RA treatment. In contrast, pulsatile dry cupping can stimulate acupuncture points without puncturing the skin, therefore is noninvasive compared to by acupuncture and the use of Humira.

Cupping, like acupuncture, is less expensive than the cost of the drug Humira. According to the British Acupuncture Council, cupping tends to run between “£40[\$52.40] to £50 [\$65.50] a session—lasting from half an hour to 40 minutes. The number of sessions needed is determined by the therapist” (1). This cost would equate to around \$786 per year, making cupping the cheapest of the three treatments. However, cupping is the hardest of the three options to obtain because it is not wide spread across the United States, with only one location in some states. However, due to its low cost and only side effect of bruising, pulsatile dry cupping should be an alternative to Humira.

Conclusion

From the evidence presented in this research paper, Humira, electro-acupuncture, and pulsatile dry cupping treatment all decrease the levels of TNF in the human body. This reduction in TNF leads to reduced osteoclast formation and therefore a minimization of swelling in Rheumatoid Arthritis patients. However, due to the various side effects of the treatments, each form of treatment should not be considered as equal.

When looking at the costs and locations of these three treatments, Humira and acupuncture are the most expensive and therefore pulsatile dry cupping should be the patient's first option. The only caveat to this is that cupping is the hardest form of treatment to find in the United States. In addition, if the patient is house bound, Humira should be the primary form of treatment. In contrast, acupuncture would be the easiest to find and is the second cheapest option of treatment.

When looking solely at the patient's health, Humira should be the last remedy to treat the symptoms of RA. While Humira has been proven to lower TNF factors and helps many people with inflammation associated with RA, the side effects can be life-threatening and potentially life-altering. Any drug that is "believed to reduce host immune responses to malignancy, thereby indirectly increasing the risk of secondary cancers" (Park 261), should not be used by the general public. One might argue that the onset of cancer is considered an 'uncommon' side effect, and therefore Humira should still be taken. However, "headache, stuffy nose, sinus pain, mild stomach pain" (Physician's Desk Reference 1), are common in patients who take Humira and can negatively impact a patient's health and ability to function normally. Furthermore, any drug that 'reduces host immune responses' and will give RA patients a "higher chance for getting a kind of cancer called lymphoma" (Food and Drug Administration 3196923) can cause side effects that may not appear until after the patient has stopped taking Humira.

Therefore, the two best options for RA treatment in terms of health for the patient are pulsatile dry cupping and electro-acupuncture. This is because pulsatile dry cupping may cause, "ecchymosis, a discolouration of the skin caused by the escape of blood into the tissue from ruptured blood vessels" (Tham 2192), and electro-acupuncture may cause "discomfort consisted of nausea or small tingling pain where the needle was injected" (Ouyang 508), which are byproducts that will last only a few weeks, at most. In contrast, the use of Humira can cause deleterious effects such as cancers that may last a lifetime. In comparing acupuncture to pulsatile dry cupping, pulsatile dry cupping may be better than electro-acupuncture because there is a greater chance of contracting a blood disease from electro-acupuncture since the doctor that administers the treatment must pierce the skin in order to perform the treatment whereas pulsatile dry cupping

does not involve piercing the skin.

In conclusion, of the three treatment methods reviewed, Humira is the least desirable because it has the worst side effects and also costs the most per month. In contrast, both electro-acupuncture and pulsatile dry cupping are significantly cheaper than Humira and are safer because they are not associated with significant long-term side effects. However, between electro-acupuncture and pulsatile dry cupping, cupping is not readily available in the United States and thus acupuncture is concluded to be the best method for RA treatment.

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